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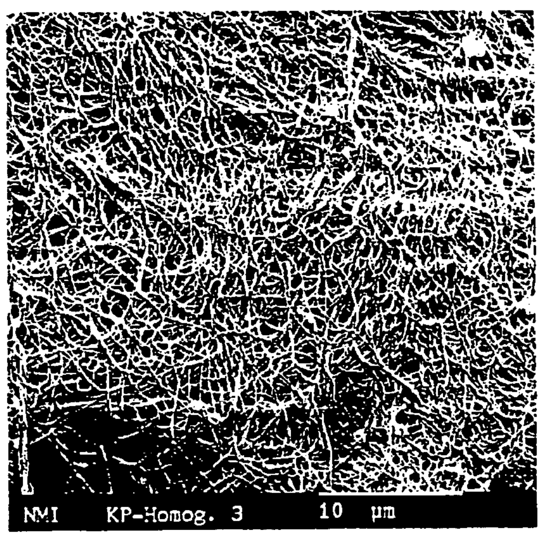
(54) **INSTRUMENT MEDICAL PERMETTANT DE MIEUX FIXER A LA PEAU LES CATHETERS A DEMEURE ET D'AUTRES IMPLANTS TRANSCUTANES TOUT EN REDUISANT LE RISQUE D'INFECTION**

(54) **MEDICAL DEVICE FOR IMPROVING SKIN FIXATION OF INDWELLING CATHETERS AND OTHER TRANSCUTANEOUS IMPLANTS WITH A REDUCED RISK OF INFECTION**



(57) Le brevet décrit un instrument médical tel qu'un cathéter dont la surface est recouverte d'un matériau fibreux avec des fibres de collagène libres ayant une structure naturelle. On y décrit également un mode d'application du matériau fibreux sur la surface de l'instrument médical et une méthode de production de matériau fibreux sur la surface de l'instrument médical. Grâce au matériau fibreux, l'instrument médical peut être fixé sur ou dans le corps humain et une infection bactérienne peut être prévenue.

(57) Disclosed is a medical device such as a catheter having on its surface a fibrous material with free collagen fibers having a natural structure. Furthermore, disclosed is a process for applying the fibrous material to the surface of the medical device and to the production of the fibrous material on the surface of the medical device. Due to the presence of the fibrous material, the medical device can be fixed in or to a living body and infection due to bacteria can be prevented.

Industrie Canada Industry Canada

ABSTRACT OF THE DISCLOSURE

Disclosed is a medical device such as a catheter having on its surface a fibrous material with free collagen fibers having a natural structure. Furthermore, disclosed is a process for applying the fibrous material to the surface of the medical device and to the production of the fibrous material on the surface of the medical device. Due to the presence of the fibrous material, the medical device can be fixed in or to a living body and infection due to bacteria can be prevented.

MEDICAL DEVICE FOR IMPROVING SKIN FIXATION OF INDWELLING CATHETERS AND OTHER TRANSCUTANEOUS IMPLANTS WITH A REDUCED RISK OF INFECTION

The present invention relates to transcutaneous medical devices and to a process for their production.

Transcutaneous medical devices are implants which pass through the skin and remain in the body for a lengthy period, such as, for example, indwelling catheters.

Examples of transcutaneous implants are catheters for peritoneal dialysis and catheters for long-term perfusion therapies. With long-term use of these and other implants, there is a risk of infection through bacteria or other micro-organisms entering the body. Various movements of the body can exert transient tensile and compressive forces on the passages for the implants through the skin, whereby fissures periodically form at the interface between the passage through the skin and the skin tissue, through which microorganisms can enter and infect the body.

Several proposals for fixation of transcutaneous implants and prevention of infections with transcutaneous devices such as, for example, catheters for peritoneal dialysis using cuffs are disclosed in the literature.

Cuffs are hollow cylinders which are a few milli-meters to a few centimeters long around the catheter. They are placed on the catheter, singly or multiply, by pulling on or by sticking on an appropriate tape. The task of the cuff is to enter with its outer surface into close contact with the

body tissue and thus fix the catheter and prevent microorganisms migrating in at the catheter/body tissue interface. To achieve this aim, the outside of the cuff consists according to U. S. Patent 5,057,075 of Dacron, of a material regarded as compatible with the body or of a porous material (U. S. Patent 5,308,338; U. S. Patent 5,141,499), into which body cells can grow.

As an additional measure to prevent microbial infections entering the body through the passage through the skin, cuffs are occasionally employed in combination with antiseptic substances. U. S. Patent 5,308,338 discloses a tube which passes inside the catheter and through which antiseptic liquids can be delivered to the cuff material.

U. S. Patent 5,049,140 describes the use of anti-microbial substances in the cuff material.

Further patents disclosing a fixation and/or prevention of infection in connection with the use of transcutaneous catheters are, for example: U. S. Patent 5,098,413; U. S. Patent 5,057,075; U. S. Patent 4,772,269; U. S. Patent 4,687,471 and U. S. Patent 4,623,329. The priority descriptions are of particular geometric embodiments of catheters for individual types of use.

Although the use of cuffs in the prior art can extend the period after which the catheter must be changed owing to signs of infection, the problems of fixation and prevention of infection of transcutaneous devices for long-term use have not yet been satisfactorily solved. In particular, the growing-in

of body tissue into porous materials does not result in a durable connection reliably preventing the penetration of infectious organisms. The use of antimicrobial and/or antiseptic substances is to be regarded as a temporary measure which is susceptible to failure and difficult to implement.

Collagen-containing composite materials are known from a different technical area to be materials which readily form adhesions to the human body (German Patent 36 327 316).

A primary object of the present invention is to make it possible to fix medical devices in or on the body and thus to prevent an infection entering the body through the passage into the body.

It has been found, surprisingly, that transcutaneous medical devices which have on their surface a fibrous material with free collagen fibers which have a natural structure prevent to a high degree a microbial infection entering the body through the point where the transcutaneous medical device passes through the skin.

The body tissue forms adhesion, without infection or rejection, with the collagen fibers of the transcutaneous medical device and thus forms a durable unit with the transcutaneous medical device. This blocks entry of infectious organisms into the body.

The present invention therefore provides a transcutaneous medical device which has on its surface a fibrous material having free collagen fibers which have a natural structure. The device is preferably a catheter. The

fibrous material may be in the form of a felt having on its surface free (or exposed or uncovered) fibers of the collagen.

The present invention furthermore provides a process for producing the transcutaneous medical device, which comprises applying to its surface a fibrous material having free collagen fibers which have a natural structure.

According to a preferred embodiment of the present invention, in the transcutaneous medical device defined above, the fibrous material is prepared by:

production of a collagen felt from collagen fibers having a natural structure;

infiltration of this felt with a polymerizable monomer;

carrying out a free-radical polymerization in the presence of a polymerization inhibitor which acts from a surface of the infiltrated felt; and

detachment of a not completely polymerized surface layer of the resulting polymer to expose the collagen fibers by using a suitable solvent.

The present invention furthermore describes a process for applying a fibrous material to a transcutaneous medical device, which process comprises:

production of a collagen felt from collagen fibers having a natural structure;

infiltration of this felt with a polymerizable monomer;

carrying out a free-radical polymerization in the

presence of a polymerization inhibitor which acts from a surface of the infiltrated felt;

detachment of a not completely polymerized surface layer of the resulting polymer to expose the collagen fibers by using a suitable solvent to produce a fibrous material; and

subsequent application of the fibrous material to a surface of the transcutaneous medical device.

The fibrous material comprises a collagen-containing composite material whose surface forms a felt of free collagen fibers having a natural structure. This collagen/polymer composite material may be produced by first obtaining, for example, as disclosed in German Patent Publication "Biocompatible composite material and process for its production" (German Application 195 29 036.4), a felt from free collagen fibers having a natural structure, and subsequently infiltrating with a polymerizable monomer preparation. If the monomer preparation contains no polymerization initiator, the polymerization may be started for example by radiation induction. The polymerization must in all cases be carried out with surface quenching. This results in a collagen-containing composite material with an incompletely polymerized layer on the surface. This layer is detached with a suitable solvent to expose the collagen fibers. It is possible to influence the thickness and characteristics of the surface layer which is not cured during the polymerization by the choice of quenching parameters.

According to another embodiment of the present invention, in the transcutaneous medical device defined above,

the fibrous material is prepared by:

production of a collagen felt from collagen fibers having a natural structure;

infiltration of this felt with a polymerizable monomer;

application of the felt infiltrated in this way to a surface of the transcutaneous medical device;

carrying out an incomplete free-radical polymerization in the presence of a polymerization inhibitor which acts from a surface of the infiltrated felt; and

detachment of the incompletely polymerized surface layer of the resulting polymer to expose the collagen fibers by using a suitable solvent.

Besides application of the fibrous material to the transcutaneous medical device, this material may also be produced directly on a surface of the transcutaneous medical device.

Another embodiment of the invention is a process for applying a fibrous material to the surface of a transcutaneous medical device, which process comprises:

production of a collagen felt from collagen fibers having a natural structure;

infiltration of this felt with a polymerizable monomer;

application of the felt infiltrated in this way to a surface of the transcutaneous medical device;

carrying out an incomplete free-radical polymerization in the presence of a polymerization inhibitor which acts

from a surface of the infiltrated felt; and

detachment of the incompletely polymerized surface layer of the resulting polymer to expose the collagen fibers by using suitable solvents.

Brief Description of the Drawings

Fig. 1 is a section through the skin (from Faller, A: der Körper des Menschen, 5th edition, Thieme, Stuttgart 1972), and diagrammatic representation of a catheter with a cuff-like device for fixation in the skin.

Fig. 2 is a microphotograph of the fibrous material used in the subcutaneous medical device according to one preferred embodiment of the present invention.

Detailed Description of the Invention

A very preferred feature of the present invention is to use special materials in the transcutaneous medical devices. These collagen/polymer composite materials have on their surface free collagen fibers having a natural structure. By "free" is meant that the collagen fibers are exposed outwards without being covered by the polymer. These composite materials are presumably responsible for the surprisingly rapid and complete incorporation and adhesion of these materials to body tissue such as, for example, cutaneous connective tissue. Transcutaneous medical devices which comprise these collagen/-polymer composite materials at specific points, for example in the form of cuffs, form adhesions via these materials to the body tissue. This results in fixation of the transcutaneous device on or in the body and, if these collagen/polymer

composite materials are located where the transcutaneous device passes through the body, impedes migration of microbial infectious organisms into the body (see Fig. 1).

In Fig. 1, the reference symbols and the reference numbers have the following meanings.

a. Epithelial layer (epidermis). b. True skin (corium), layer with connective tissue papillae (stratum papillare). c. Reticular layer of the true skin (stratum reticulare). d. Subcutaneous fatty tissue. 1. Meissner's corpuscle. 2. Opening of a sweat gland on a ridge. 3. Free nerve fiber. 4. Convolution of the sweat gland. 5. Lamellated corpuscle (Vater-Pacini) in longitudinal section. 6. Cornified layer (stratum corneum). 7. Cornifying layer (stratum granulosum and stratum lucidum). 8. Layer of living epithelial cells (stratum germinativum). 9. Capillary loops in the connective tissue papillae. 10. Cut surface of a small nerve. 11. Interlaced bundles of connective tissue in the true skin. 12. Efferent duct of a sweat gland. 13. Cross-section through a lamellated corpuscle. 14. Fatty tissue lobules. 15. Catheter in section. 16. Cuff made of the collagen/plastic composite material. 17. Region of adhesion to the true skin.

In Fig. 1, the top indicates outside of the body (i. e. skin) and the bottom indicates inside of the body.

<u>Use of a Fine-fiber Collagen</u>

The property which causes the implant material according to the invention to form adhesions with the skin results from the fine collagen fibers which are anchored in

the implant material and project out of the implant surface. These fibers have a diameter of up to 500, preferably of up to about 200, nm, and correspond in their structure to natural collagen (see Fig. 2). The collagen fibers formed by human cells are therefore able readily to unite with the collagen fibers of the composite material and ensure favorable incorporation of the transcutaneous medical devices with the body tissue.

Usual commercially obtainable collagen products are more or less denatured with loss of their native structure.

The following process can be used to produce fine-fiber collagen having a natural structure. Collagen, for example from bovine or rat tail tendons, is dissolved in a weak acid such as dilute acetic acid and then purified, preferably by dialysis and centrifugation. The centrifuge supernatent containing the collagen molecules is then removed and transferred into sterile vessels. Alteration of the pH and of the salt concentration results in the collagen molecules becoming organized in felt-like mats of fine-fiber collagen.

Production of the Collagen/Polymer Composite Materials

Crucial for successful application of a collagen-containing composite material is exposure of the native collagen fibers on the surface during production.

This may be achieved with the material described herein by impregnation of the collagen mats (or felts) with curable monomers for example methyl methacrylate (MMA), subsequent free-radical polymerization (curing) in the presence of polymerization inhibitors which act out from the surface of

the impregnated collagen mats, and then removal of the top most layer of the collagen/polymer composite material for partial exposure of the collagen fibers (exposed felt).

A process which is based on the principle of inhibition of the polymerization reaction at the surface by oxygen is preferably used. In this process, the collagen mats impregnated with a monomer are polymerized not in closed molds but with access for oxygen or for an oxygen-containing gas mixture. Since polymerization reactions can be inhibited by oxygen, an uncured outer layer remains on the surface of the samples and is subsequently removed by treatment with a suitable solvent, for example acetone. It is possible in this way to expose the collagen fibers on the surface. The thickness of the layer can be controlled by a choice of the appropriate parameters (oxygen concentration, duration of the curing process, light intensity, temperature, solvent).

It is possible in principle to use as curable monomers all substances, singly (homopolymers) or in combination with other monomers (copolymers), which polymerize by a free-radical reaction, such as, for example, styrene, vinyl compounds, maleic anhydride or alkyl acrylates and methacrylates, where the alkyl group may contain 1 to 12 C atoms. The structure can be linear, branched, cycloaliphatic, aromatic or substituted aromatic. It is furthermore possible to use heterocyclic monomers which have either nitrogen, sulfur or oxygen in the side chain. The monomers can be used as single components or in the form of monomer mixtures or monomer/polymer mixtures with or without fillers.

The polymerizable monomer mixture may contain monomers capable of free-radical polymerization, preferably (meth)acrylates, particularly preferably methacrylates.

The polymerizable monomer mixture may furthermore contain one or more compounds from the following group: methyl methacrylate, ethyl methacrylate, n-butyl methacrylate, isobutyl methacrylate, 2-ethylhexyl methacrylate, cyclohexyl methacrylate, isobornyl methacrylate, tetrahydro-furfuryl methacrylate, benzyl methacrylate, morpholinoethyl methacrylate, diethylene glycol dimethacrylate, triethylene glycol dimethacrylate, diurethane dimethacrylate (product of the reaction of trimethylhexamethylene diisocyanate with two moles of 2-hydroxyethyl methacrylate), isopropylidenebis(2(3)-hydroxy-3(2)-(4-phenoxy)propyl methacrylate) and/or methacrylic acid.

In addition, the polymerizable monomer mixture may contain one or more compounds from the following group: styrene, α-methylstyrene, styrenesulfonic acid, vinyl compounds and/or maleic anhydride.

Vinyl compounds may be ethylene, propylene or butylenes, but also vinyl chloride or butadiene. Other components of the monomer mixture may be solvents and/or fillers, and polymerization initiators.

Polymerization initiators which can be used include azo nitriles, alkyl peroxides, acyl peroxides, hydroperoxides, peroxo ketones, peresters and peroxocarbonates, peroxodisulfate, persulfate and all usual photoinitiators.

The polymerization can likewise be initiated thermally or by electromagnetic

radiation such as, for example, UV light or γ radiation.

To produce an incompletely polymerized layer on the surface of the collagen composite material, the polymerization is carried out in the presence of oxygen or of an oxygen-containing gas mixture. The incompletely polymerized layer produced in this way is detached with a suitable solvent such as, for example, acetone, methyl ethyl ketone, acetonitrile or THF.

There are several possibilities for applying, according to the invention, materials which have been obtained in this way and have free collagen fibers to a surface of bodies of transcutaneous medical devices:

application of the still plastic material, that is to say a mixture of monomers and collagen, to a body of a medical device with subsequent surface-quenched curing and detachment of the incompletely polymerized surface;

production of hollow cylinders, for example by infiltration of the collagen felt in the wall space of a mold. The highly viscous monomer/collagen material is then removed from the mold, impaled on a spike and polymerized with surface quenching in oxygen or an oxygen-containing gas mixture. After detachment of the incompletely polymerized outer layer with a solvent, this results in hollow cylinders of the polymer/collagen composite material with a smooth inside and an outside with free collagen fibers. Hollow cylinders with various dimensions can be produced by choice of different molds. The molds preferably used have:

a length of from 0.2 to 7 cm;

an external diameter of from 0.5 to 2 cm;

an internal diameter of from 0.2 to 1.5 cm.

Hollow cylinders which have free collagen fiber ends on the outside and which have been produced in this or another way can be employed in various embodiments for the fixation of transcutaneous implants, for example as:

a cuff which is drawn over the catheter and fixed at the required point by annular tension forces, use of a biocompatible adhesive such as, for example, histoacrylic adhesive or in other ways;

a sheath which is fitted via socket connectors into the catheter; and

a sheath which is fixed vertically in the skin and is left for some weeks to incorporate into the cutaneous tissue. Then a catheter is pushed through the sheath, and the annular gap between the catheter and the inner wall of the sheath is sealed with silicone oil or another suitable material.

To assist the incorporation process in the use according to the invention of the collagen/polymer composite materials for transcutaneous medical devices, the surface of the transcutaneous device can be coated, shortly before its use, with a gel which may contain antibiotics, substances promoting tissue growth and/or other active substances. To prepare this gel, an aqueous solution or suspension of the active substances is prepared and is then solidified by adding gel-forming substances.

Constituents of the gel

Antibiotics

Antibiotics are employed in the gel formation in an amount which, taking account of diffusion losses, prevents sepsis for several days. Particularly suitable antibiotics are penicillin, streptomycin and other, mainly lipophilic antibiotics.

Growth factors

Adequate amounts of a commercially available epidermal growth factor or other factors such as, for example, fibroblast growth factor or platelet derived growth factor are added. It may be advantageous to add dextran or calcium phosphate together with the growth factors in order to achieve a release-slowing effect (European Patent No. 530,458, Japanese Patent Publication No. 6 3-105765).

Formation of the gel

The aqueous solution or suspension containing the active substances can be converted into a gel in several ways:

- addition of fibrinogen, thrombin and aprotinin;
- addition of collagen as disclosed by Parson-Wingerter and Saltzman (Biotechnol. Prog. 9, pages 600 - 607/1993);
- addition of a mixture of collagen and calcium phosphate; and
- addition of sodium alginate and subsequent initiation of gel formation by addition of $CaCl_2$.

The following example is intended to illustrate the invention in detail:

18 cylindrical specimens (diameter: 4 mm, length: 15 mm) were implanted dorsally in two rows subcutaneous from cranial to caudal in 3 young male rats. These 18 specimens consisted of:

- 3 × poly(methyl methacrylate) (PMMA);
- 6 × PMMA/collagen composite material, collagen fibers not crosslinked;
- 6 × PMMA/collagen composite material, collagen fibers crosslinked with

glutaraldehyde; and

- 3 × polytetrafluoroethylene.

The collagen-containing specimens were produced as follows: collagen having a natural structure was infiltrated with a methyl methacrylate monomer mixture (see German Application 195 29 036.4) and then cured in a bowl-shaped curing mold under a halogen lamp with a radiation maximum at 340 nm for 10 min. This curing was carried out in a desiccator which had previously been flushed with oxygen. The samples were then immersed with agitation in acetone for 10 min to detach the uncured surface layer. To produce the specimens with crosslinked collagen, the collagen having a natural structure was fixed with glutaraldehyde before infiltration with the monomer mixture.

Since the oxygen had access only to that part of the sample surface which was on top in the bowl-shaped curing mold during the curing, in the subsequent acetone treatment free collagen fibers were exposed only on this part of the surface (almost 50% of the total surface).

All the specimens were incorporated without rejection and inflammation into the cutaneous tissue. However, the determination of the tensile forces necessary to extract the implants from the cutaneous tissue of the sacrificed rats, which was carried out after 28 days, showed marked differences:

Material	Average tensile forces used to extract the specimens [N]
Polytetrafluoroethylene	< 1.0
PMMA	3.0
PMMA/collagen composite material, not crosslinked	6.5
PMMA/collagen composite material, crosslinked	5.7

The forces to be used to extract the specimens in the case of the collagen-containing composite materials show the good union of the specimens with the body tissue, especially since the free collagen fibers are exposed only on almost 50% of the total surface of the specimens.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A transcutaneous medical device which has on its surface a fibrous material with free collagen fibers which have a natural structure.

2. The medical device according to claim 1, wherein the fibrous material is prepared by:

production of a collagen felt from collagen fibers having a natural structure;

infiltration of this felt with a polymerizable monomer;

carrying out a free-radical polymerization in the presence of a polymerization inhibitor which acts out from a surface of the infiltrated felt; and

detachment of an incompletely polymerized surface layer of the resulting polymer to expose the collagen fibers by using a suitable solvent.

3. The medical device according to claim 1, obtainable by:

production of a collagen felt from collagen fibers having a natural structure;

infiltration of this felt with a polymerizable monomer;

application of the felt infiltrated in this way to a surface of the transcutaneous medical device;

carrying out a free-radical polymerization in the

presence of a polymerization inhibitor which acts out from a surface of the infiltrated felt; and

detachment of an incompletely polymerized surface layer of the resulting polymer to expose the collagen fibers by using a suitable solvent.

4. The medical device according to claim 2 or 3, wherein the polymerizable monomer comprises a monomer capable of free-radical polymerization.

5. The medical device according to claim 2, 3 or 4, wherein the polymerizable monomer comprises an acrylate.

6. The medical device according to claim 2, 3 or 4, wherein the polymerizable monomer comprises a methacrylate.

7. The medical device according to claim 2, 3 or 4, wherein the polymerizable monomer comprises one or more compounds selected from the group consisting of:

methyl methacrylate, ethyl methacrylate, n-butyl methacrylate, isobutyl methacrylate, 2-ethylhexyl methacrylate, cyclohexyl methacrylate, isobornyl methacrylate, tetrahydrofurfuryl methacrylate, benzyl methacrylate, morpholinoethyl methacrylate, diethylene glycol dimethacrylate, triethylene glycol dimethacrylate, diurethane dimethacrylate (product of the reaction of trimethylhexamethylene diisocyanate with two moles of 2-hydroxyethyl methacrylate), isopropylidenebis(2(3)-hydroxy-3(2)-(4-phenoxy)propyl methacrylate) and methacrylic acid.

8. The transcutaneous medical device according to claim 7, wherein the polymerizable monomer is methyl methacrylate.

9. The medical device according to claim 2, 3 or 4, wherein the polymerizable monomer comprises one or more compounds selected from the group consisting of styrene, α-methylstyrene, styrenesulfonic acid, ethylene, propylene, butylene, vinyl chloride, butadiene and maleic anhydride.

10. The medical device according to any one of claims 2 to 9, wherein the polymerization inhibitor is oxygen.

11. The medical device according to any one of claims 2 to 10, wherein the collagen felt is produced by:

a) dissolving collagen in a weak acid;
b) purifying the collagen; and
c) adjusting the pH and salt concentration.

12. The medical device according to any one of claims 1 to 11, wherein the device is a catheter.

13. A process for producing a medical device having a surface coated with a fibrous material, which process comprises applying to a surface of the device a fibrous material comprising free collagen fibers having a natural structure.

14. The process according to claim 13, wherein the fibrous material is produced by:

production of a collagen felt from collagen fibers having a natural structure;

infiltration of this felt with a polymerizable monomer;

carrying out a free-radical polymerization in the presence of a polymerization inhibitor; and

detachment of a resulting polymer to expose the collagen fibers by using a solvent.

15. The process according to claim 14, wherein the fibrous material is applied to the surface of the medical device by:

production of a collagen felt from collagen fibers having a natural structure;

infiltration of this felt with a polymerizable monomer;

application of the felt infiltrated in this way to a surface of the transcutaneous medical device;

carrying out a free-radical polymerization in the presence of a polymerization inhibitor; and

detachment of a resulting polymer to expose the collagen fibers by using suitable solvents.

16. A process according to any one of claims 13 to 15, wherein the polymerizable monomer comprises a monomer capable of free-radical polymerization.

17. A process according to any one of claims 13 to 15, wherein the polymerizable monomer comprises an acrylate.

18. A process according to any one of claims 13 to 15, wherein the polymerizable monomer comprises a methacrylate.

19. A process according to any one of claims 13 to 15, wherein the polymerizable monomer comprises one or more compounds selected from the group consisting of:

methyl methacrylate, ethyl methacrylate, n-butyl methacrylate, isobutyl methacrylate, 2-ethylhexyl methacrylate, cyclohexyl methacrylate, isobornyl methacrylate, tetrahydrofurfuryl methacrylate, benzyl methacrylate, morpholinoethyl methacrylate, diethylene glycol dimethacrylate, triethylene glycol dimethacrylate, diurethane dimethacrylate (product of the reaction of trimethylhexamethylene diisocyanate with two moles of 2-hydroxyethyl methacrylate), isopropylidenebis(2(3)-hydroxy-3(2)-(4-phenoxy)propyl methacrylate) and methacrylic acid.

20. A process according to any one of claims 13 to 15, wherein the polymerizable monomer comprises one or more compounds selected from the group consisting of styrene, α-methylstyrene, styrenesulfonic acid, ethylene, propylene, butylene, vinyl chloride, butadiene and maleic anhydride.

21. The process according to any one of claims 14 to 20, wherein the polymerization inhibitor is oxygen.

22. The process according to any one of claims 14 to 21, wherein the collagen felt is produced by:

a) dissolving collagen in a weak acid;

b) purifying the collagen; and

c) adjusting the pH and salt concentration.

23. The process according to any one of claims 13 to 22, wherein the device is a catheter.

24. A transcutaneous medical device which comprises:

a body of the medical device, and

a fibrous material covering at least such a part of a surface of the body that remains in a human body when the medical device is in use,

wherein the fibrous material is a felt made of a composite material of a polymer and fine fibers of collagen having a natural structure and a diameter of not more than 500 nm; and

the felt has, on its surface, the collagen fine fibers which are anchored in the felt and are exposed outwards without being covered by the polymer.

25. A transcutaneous medical device according to claim 24, wherein the medical device is a catheter and the fibrous material is a cuff or a sheath.

26. A transcutaneous medical device according to claim 24 or 25, wherein fibrous material is produced by (1) a free-radical polymerization of a polymerizable monomer in a felt of the collagen fibers infiltrated with the polymerizable monomer in the presence of a polymerization inhibitor which acts from a surface of the infiltrated felt and (2) detaching an incompletely polymerized surface layer of the resulting

polymer by using a solvent to expose the free ends of the collagen fibers.

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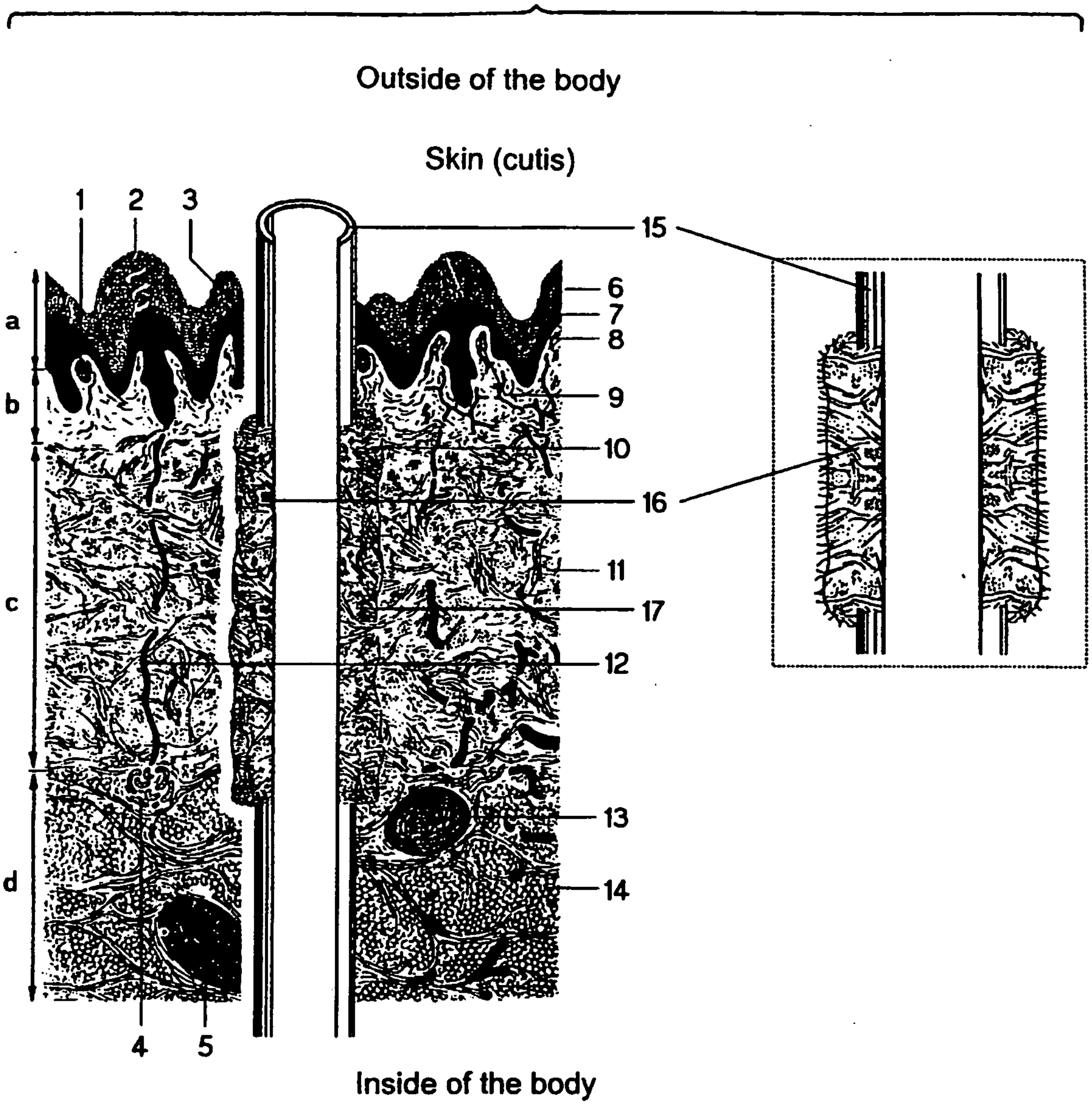
FIG. 1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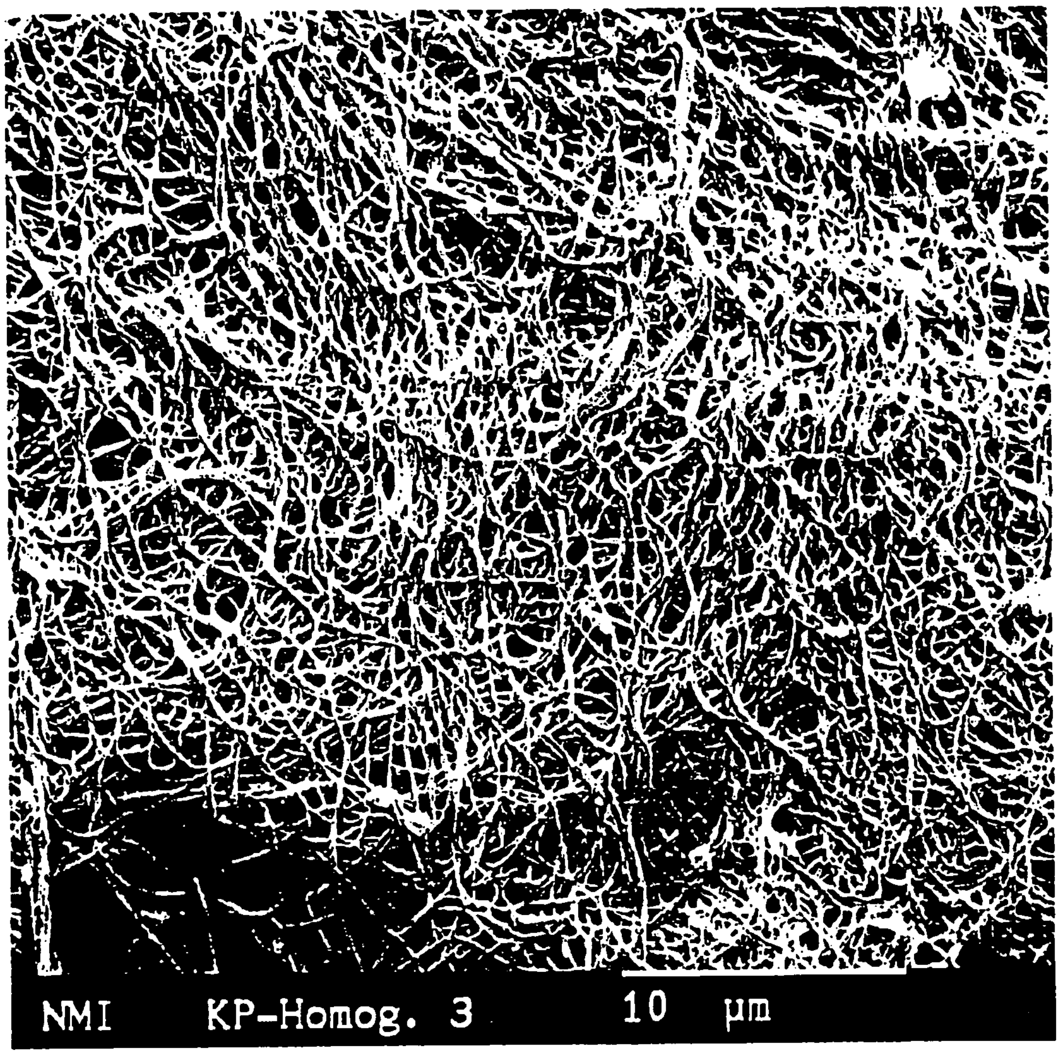
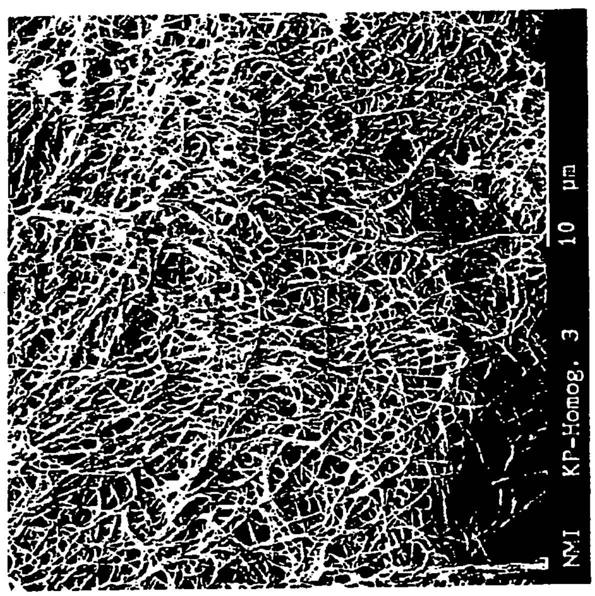


FIG. 2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